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     (FILE 'HOME' ENTERED AT 19:48:33 ON 30 MAR 2008)

     FILE 'CAPLUS, MEDLINE, BIOSIS' ENTERED AT 19:48:55 ON 30 MAR 2008
L1          2871 S OXYMETAZOLINE
L2           452 S L1 (P) (NASAL? OR DECONGEST?)
L3            36 S L2 (P) (LIPOSOME OR PRESERVATIVE OR CAMPHOR OR MENTHOL OR EUC
L4             0 S L3 AND (VISCO? OR THICKEN?)
L5             1 S L3 AND GEL
L6            25 DUP REM L3 (11 DUPLICATES REMOVED)
L7            17 S L6 NOT PD>20020913
L8            16 S L7 NOT L5

=> d que L3
L1          2871 SEA OXYMETAZOLINE
L2           452 SEA L1 (P) (NASAL? OR DECONGEST?)
L3            36 SEA L2 (P) (LIPOSOME OR PRESERVATIVE OR CAMPHOR OR MENTHOL OR
                 EUCALYPTUS OR AZULEN OR BUFFER)


=> d L8 1-16 TI ABS IBIB

L8   ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2008 ACS on STN
TI   Adverse effects of benzalkonium chloride on the nasal mucosa: allergic
     rhinitis and rhinitis medicamentosa
AB   Prolonged, repeated use of nasal decongestants for
     symptomatic relief of allergic rhinitis often results in rhinitis
     medicamentosa (RM), a condition involving "rebound swelling" and addnl.
     congestion.  Most decongestant sprays contain the
     preservative benzalkonium chloride (BKC), which causes toxic
     reactions in the nose, eyes, ears, and lungs, and may exacerbate the
     symptoms of allergic rhinitis.  Recent studies demonstrate the effects of
     nasal sprays containing BKC or the decongestant
     oxymetazoline (OXY) in the development of RM.  Using
     rhinostereometry, a technique that measures nasal mucosal
     swelling and nasal reactivity (with histamine challenge tests),
     prolonged use of OXY has been shown to induce nasal mucosal
     swelling and hyperreactivity.  Sustained use of BKC alone induces
     nasal mucosal swelling and, in combination with OXY, BKC appears
     to have a long-term adverse effect on nasal mucosa.  Its
     presence may also contribute to the RM resulting from overuse of
     decongestant sprays.  Addnl. research is needed to confirm the
     deleterious effects of BKC in nasal products.  However, these
     potential effects may be points of clin. differentiation in the treatment
     of allergic rhinitis and prevention of RM.
ACCESSION NUMBER:        1999:750604  CAPLUS
DOCUMENT NUMBER:         131:331875
TITLE:                   Adverse effects of benzalkonium chloride on the nasal
                         mucosa: allergic rhinitis and rhinitis medicamentosa
AUTHOR(S):               Graf, Peter
CORPORATE SOURCE:        Department of Otorhinolaryngology, Karolinska
                         Institute, Huddinge University Hospital, Huddinge,
                         Swed.
SOURCE:                  Clinical Therapeutics (1999), 21(10), 1749-1755
                         CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER:               Excerpta Medica, Inc.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         22    THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L8 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Effect on the nasal mucosa of long-term treatment with oxymetazoline, benzalkonium chloride, and placebo nasal sprays
AB A parallel, randomized, double-blind study was performed in healthy subjects to investigate the effects on the nasal mucosa of a 1-mo treatment with nasal sprays. Some subjects received oxymetazoline nasal spray; others used a nasal spray containing the preservative benzalkonium chloride, and still others were treated with a placebo nasal spray. The 3 variables that were studied (nasal mucosal swelling, symptom scores, and nasal reactivity) were estimated by histamine challenge before and after 28 days of treatment. Rhinostereometry was used to measure nasal mucosal swelling and nasal reactivity. After 28 days of use, benzalkonium chloride spray induced an increase in nasal mucosal swelling. At the end of the month, the score for nasal stuffiness was higher for the persons treated with oxymetazoline than for those treated with benzalkonium chloride. Oxymetazoline nasal spray induced a pronounced increase in nasal reactivity, greater than that induced in the placebo group. Long-term use of placebo and benzalkonium chloride nasal sprays also caused an increase in nasal reactivity, but not to the same extent as did the nasal sprays containing oxymetazoline. It is concluded that long-term use of oxymetazoline induces a sensation of nasal stuffiness, which may be due to unconscious exaggeration of the degree of nasal stuffiness, induced nasal hyperreactivity, or a combination of both. These factors are probably the main reasons for the prolonged use of nasal decongestive sprays and the development of rhinitis medicamentosa. Benzalkonium chloride induces mucosal swelling, which explains why the presence of this preservative in a decongestant spray aggravates rhinitis medicamentosa.
ACCESSION NUMBER: 1997:31547 CAPLUS
DOCUMENT NUMBER: 126:70099
TITLE: Effect on the nasal mucosa of long-term treatment with oxymetazoline, benzalkonium chloride, and placebo nasal sprays
AUTHOR(S): Graf, Peter; Hallen, Hans
CORPORATE SOURCE: Department Otorhinolaryngology, Karolinska Institute, Stockholm, Swed.
SOURCE: Laryngoscope (1996), 106(5, Pt. 1), 605-609
CODEN: LARYA8; ISSN: 0023-852X
PUBLISHER: American Laryngological, Rhinological and Otological Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Nasal spray compositions containing oxymetazoline
AB An aqueous nasal decongestant composition containing oxymetazoline is disclosed which does not contain mercurial preservatives. A preserved mercurial-free aromatic nasal spray was formulated containing 0.05% oxymetazoline-HCl and 0.25% benzyl alc. enabling a 90.9% reduction in solubilizing agent.
ACCESSION NUMBER: 1995:737642 CAPLUS
DOCUMENT NUMBER: 123:123213
TITLE: Nasal spray compositions containing oxymetazoline
INVENTOR(S): Haslwanter, Joseph A.; Rencher, William
PATENT ASSIGNEE(S): Schering-Plough Healthcare Products Inc., USA
SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9513810	A1	19950526	WO 1994-US12945	19941117
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9510931	A	19950606	AU 1995-10931	19941117
US 5854269	A	19981229	US 1996-640767	19960806
PRIORITY APPLN. INFO.:			US 1993-155052 A	19931119
			WO 1994-US12945 W	19941117

L8 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI The effect of a benzalkonium chloride-containing nasal spray on human respiratory mucosa in vitro as a function of concentration and time of action
AB Human respiratory mucosa was exposed to oxymetazoline nasal spray in varying concns. and for varying periods of time in vitro. The drug destroyed the tissue in a concentration- and time-dependent manner. In the expts. with various concns. of the spray, some tissue fragments retained their viability throughout the experiment This number increased parallel to a decrease in concns. of the test substance. All the tissue fragments exposed to undiluted nose spray underwent severe destructive alterations during the exposure period. These alterations appeared first and were most extensive in those exposed for the longest periods of time. It has previously been demonstrated that the toxic effect of oxymetazoline nasal spray in vitro is probably due to the preservative benzalkonium chloride. The apparent lack of consistency between the toxic effects of benzalkonium chloride in vitro and in vivo is discussed, with special reference to protective systems absent in vitro but present in vivo.
ACCESSION NUMBER: 1995:512127 CAPLUS
DOCUMENT NUMBER: 122:256035
TITLE: The effect of a benzalkonium chloride-containing nasal spray on human respiratory mucosa in vitro as a function of concentration and time of action
AUTHOR(S): Berg, Oystein H.; Henriksen, R. N.; Steinsvaag, S. K.
CORPORATE SOURCE: Dep. of Otolaryngology, Haukeland Univ. Hospital, Bergen, Norway
SOURCE: Pharmacology & Toxicology (Copenhagen) (1995), 76(4), 245-9
CODEN: PHTOEH; ISSN: 0901-9928
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

L8 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Topical pharmaceuticals containing eriodictyon fluid extract as excipient
AB Eriodictyon fluid extract is used as excipient in topical pharmaceuticals for delivery of drugs to skin or mucosa. A nasal solution contained eriodictyon fluid extract 2.5, buffer 1.5, NaCl 5.0, oxymetazoline 1.0, and water 90.0%.
ACCESSION NUMBER: 1994:280337 CAPLUS

DOCUMENT NUMBER: 120:280337
TITLE: Topical pharmaceuticals containing eriodictyon fluid extract as excipient
INVENTOR(S): Parnell, Francis W.
PATENT ASSIGNEE(S): Parnell Pharmaceuticals, USA
SOURCE: U.S., 8 pp. Cont.-in-part of U.S. 5,128,132.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5248501	A	19930928	US 1991-667547	19910311
US 4938963	A	19900703	US 1988-275124	19881122
AU 9053397	A	19910724	AU 1990-53397	19891226
EP 507768	A1	19921014	EP 1990-905259	19891226
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
US 5015474	A	19910514	US 1990-499952	19900326
US 5128132	A	19920707	US 1990-608336	19901102
WO 9114441	A1	19911003	WO 1991-US2009	19910325
W: AU, CA, GB, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
WO 9114442	A1	19911003	WO 1991-US2018	19910325
W: AU, CA, GB, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9175834	A	19911021	AU 1991-75834	19910325
AU 9176605	A	19911021	AU 1991-76605	19910325
EP 524981	A1	19930203	EP 1991-907061	19910325
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 524987	A1	19930203	EP 1991-907188	19910325
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				

PRIORITY APPLN. INFO.:		
US 1988-275124	A2	19881122
US 1990-499952	A2	19900326
US 1990-608336	A2	19901102
WO 1989-US5818	A	19891226
US 1991-667547	A	19910311
WO 1991-US2009	A	19910325
WO 1991-US2018	A	19910325

L8 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Nasal spray products
AB A nasal spray product comprises a pump-actuated nasal dispenser equipped with a reservoir, spray head and liquid/air mixing means, wherein the reservoir contains a topical nasal medicament composition in the form of a sprayable liquid comprising a carboxyl-containing polymer, a surfactant and a pharmaceutically-acceptable nasal medicament. The product provides a high availability of active ingredient and reduces the common problem of rollback associated with drops and non-gellable nasal formulations. For example, a nasal preparation contained menthol 0.025, eucalyptol 0.0075, Carbopol-974 1.0, oxymetazoline 0.05, di-Na EDTA 0.05, methylparaben 0.065, propylparaben 0.035, Na lauryl sulfate 0.8, and water to 100%.
ACCESSION NUMBER: 1994:253408 CAPLUS
DOCUMENT NUMBER: 120:253408
TITLE: Nasal spray products
INVENTOR(S): Koochaki, Patricia Elaine; Hafner, Roderick Peter
PATENT ASSIGNEE(S): Procter and Gamble Co., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9405330	A1	19940317	WO 1993-US7554	19930812
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9458922	A	19940329	AU 1994-58922	19930812
PRIORITY APPLN. INFO.:			GB 1992-18834 A	19920905
			WO 1993-US7554 W	19930812

L8 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Inhibition of human neutrophil actin polymerization, phagocytosis and oxidative burst by components of decongestive nosedrops
AB Human neutrophil functions have been examined after exposure of leukocytes to components of decongestive nosedrops in vitro. Both the vasoactive components oxymetazoline chloride and xylometazoline chloride, as well as the preservative benzalkonium chloride, showed a concentration- and time-dependent deleterious effect on neutrophil actin polymerization, phagocytosis and oxidative burst. The most toxic of the drug components was benzalkonium chloride, which in the com. nosedrops tested was present in concns. about 20 times higher than that compatible with intact neutrophil functions. These findings suggest possible inhibition of mucosal neutrophil activity following exposure to nosedrops in vivo, and support earlier reports that have questioned the use of preservatives in decongestive nosedrops.
ACCESSION NUMBER: 1993:595451 CAPLUS
DOCUMENT NUMBER: 119:195451
TITLE: Inhibition of human neutrophil actin polymerization, phagocytosis and oxidative burst by components of decongestive nosedrops
AUTHOR(S): Bjerknes, Robert; Steinsvaag, Sverre Karmhus
CORPORATE SOURCE: Dep. Paediatr., Univ. Bergen, Bergen, N-5021, Norway
SOURCE: Pharmacology & Toxicology (Oxford, United Kingdom) (1993), 73(1), 41-5
CODEN: PHTOEH; ISSN: 0901-9928
DOCUMENT TYPE: Journal
LANGUAGE: English

L8 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Nose drops. Effects of drugs on the vibratory frequency of nasal ciliae
AB Studies of the toxicity of nasally applied decongestants to the nasal ciliae by light-microscopic measurement of isolated human ciliae vibratory frequency before and after the application of oxymetazoline (I), I + benzalkonium chloride (BAC, a common preservative in nasal sprays) or xylometazoline (II) + BAC showed I alone to exert no significant effect, but combinations of I + BAC and II + BAC to drastically reduced vibratory frequency, indicative of ciliae damage. The effect was larger for the latter contamination and was irreversible. Wherever possible, I should thus be nasally applied without BAC present; if this is impossible (e.g. in containers containing >1 dose) the combination I + BAC is preferred to II + BAC.
ACCESSION NUMBER: 1992:584623 CAPLUS
DOCUMENT NUMBER: 117:184623
TITLE: Nose drops. Effects of drugs on the vibratory

frequency of nasal ciliae
AUTHOR(S): Deitmer, Thomas; Scheffler, Reinhard
CORPORATE SOURCE: Klin. Poliklin. Hals-, Nasen- Ohrenheilkd., Muenster, W-4400, Germany
SOURCE: Deutsche Apotheker Zeitung (1992), 132(15), 751-4
CODEN: DAZEA2; ISSN: 0011-9857
DOCUMENT TYPE: Journal
LANGUAGE: German

L8 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Nasal compositions containing anaesthetics and decongestants for the treatment of sinus headache
AB A topically applicable nasal composition capable of eliciting a therapeutic response in the mucous membranes of the sinuses comprises an anesthetically effective amount of an acid addition salt of dyclonine or pramoxine alone or in combination with an adrenergically effective amount of an acid addition salt of sympathomimetic amine decongestants. The composition is effective for reliveing sinus headache associated with inflamed and/or congested turbinates, accompanied by localized pain perceived on the septum. A composition contained thonzonium bromide 0.05, oxymetazoline-HCl 0.05, dyclonine-HCl 0.50, NaH2PO4 1.10, Na2HPO4 0.30, thimerosal 0.002, methylparaben 0.0065, propylparaben 0.0035, menthol 0.10, eucalyptol 0.02, camphor 0.02, EtOH 0.06, cetylpyridinium chloride 0.05, NaCl 0.20, polysorbate-80 0.50, and water to 100.00 %.
ACCESSION NUMBER: 1992:46329 CAPLUS
DOCUMENT NUMBER: 116:46329
TITLE: Nasal compositions containing anaesthetics and decongestants for the treatment of sinus headache
INVENTOR(S): Geria, Navin Manohar
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 454617	A1	19911030	EP 1991-810188	19910321
R: BE, DE, DK, ES, FR, GB, GR, IT				
US 5478565	A	19951226	US 1990-500610	19900327
AU 9173720	A	19911003	AU 1991-73720	19910322
AU 651089	B2	19940714		
CA 2039055	A1	19910928	CA 1991-2039055	19910326
ZA 9102281	A	19911224	ZA 1991-2281	19910326
JP 04221313	A	19920811	JP 1991-84476	19910326
PRIORITY APPLN. INFO.:			US 1990-500610 A	19900327

L8 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Inhibitory effects of nasal drops components on granulocyte chemotaxis
AB The toxic effect of components in nasal drops on chemotaxis by human granulocytes was studied. The vasoactive substances oxymetazoline chloride and xylometazoline chloride gave a successive reduction of chemotaxis down to zero for a concentration of 500 mg/L which is around that used in com. prepns. The preservative benzalkonium chloride which is used in nasal drops in a concentration of 200 mg/L was deleterious for chemotaxis at a concentration of 0.8 mg/L. Thiomersal was deleterious for chemotaxis at a concentration of 1 mg/L which

should be compared with a concentration of 24 mg/L used as preservative in nasal drops. The present results indicate that the addition of preservatives in nasal drops should be questioned.

ACCESSION NUMBER: 1989:225304 CAPLUS
DOCUMENT NUMBER: 110:225304
TITLE: Inhibitory effects of nasal drops components on granulocyte chemotaxis
AUTHOR(S): Haakansson, Bo; Forsgren, Arne; Tegner, Hans; Toremalm, Nils Gunnar
CORPORATE SOURCE: Dep. Otorhinolaryngol., Malmoe Gen. Hosp., Malmoe, S-214 01, Swed.
SOURCE: Pharmacology & Toxicology (Oxford, United Kingdom) (1989), 64(4), 321-3
CODEN: PHTOEH; ISSN: 0901-9928
DOCUMENT TYPE: Journal
LANGUAGE: English

L8 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gas chromatographic determination of some imidozolines in pharmaceutical preparation using a FFAP stationary phase
AB Tetrahydrozoline, naphazoline, xylometazoline, and oxymetazoline , present in nasal and eye drops, were determined by gas chromatog., using FFAP polar stationary phase which has high thermal stability. No failing was observed with this phase material, and the method is precise and accurate. Compds. such as neomycin, hydrocortisone, benzalhonium chloride, and menthol did not interfere with the determination

ACCESSION NUMBER: 1988:226976 CAPLUS
DOCUMENT NUMBER: 108:226976
TITLE: Gas chromatographic determination of some imidozolines in pharmaceutical preparation using a FFAP stationary phase
AUTHOR(S): Massaccesi, Maurizio
CORPORATE SOURCE: Serv. Controllo Qual., Angelini Farm., Ancona, Italy
SOURCE: Pharmaceutica Acta Helvetiae (1987), 62(10-11), 302-5
CODEN: PAHEAA; ISSN: 0031-6865
DOCUMENT TYPE: Journal
LANGUAGE: Italian

L8 ANSWER 12 OF 16 MEDLINE on STN
TI Ten days' use of oxymetazoline nasal spray with or without benzalkonium chloride in patients with vasomotor rhinitis.
AB CONTEXT: In most countries, the use of topical nasal decongestants is limited to a maximum of 10 days because of the risk of developing rebound mucosal swelling and rhinitis medicamentosa. OBJECTIVE: To determine whether topical nasal decongestants can be safely used for 10 days in patients with chronic inflammation of the nasal mucosa. DESIGN: Double-blind, randomized, controlled, parallel study. PATIENTS: Thirty-five patients with vasomotor rhinitis selected from our outpatient department. INTERVENTION: Eighteen patients received oxymetazoline hydrochloride (0.5 mg/mL) nasal spray containing the preservative benzalkonium chloride (0.1 mg/mL), and the other 17 were treated with oxymetazoline nasal spray without benzalkonium chloride. Before and after the treatment, recordings of the nasal mucosa and minimal cross-sectional area were made with rhinostereometry and acoustic rhinometry, followed by histamine hydrochloride challenge tests. Symptoms of nasal stuffiness were estimated on visual analog scales (0-100) in the morning and the evening, just before the nasal spray was used. RESULTS: No rebound swelling was found after the 10-day treatment in the 2 groups with either of the methods or as estimated by symptom scores. In the group

receiving oxymetazoline containing benzalkonium chloride, but not in the other group, the histamine sensitivity was significantly reduced after treatment (P<.001). CONCLUSIONS: It is safe to use topical nasal oxymetazoline with or without benzalkonium chloride for 10 days in patients with vasomotor rhinitis. However, this study indicates that benzalkonium chloride in nasal decongestant sprays affects the nasal mucosa also after short-term use.

ACCESSION NUMBER: 1999450341 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10522506
TITLE: Ten days' use of oxymetazoline nasal spray with or without benzalkonium chloride in patients with vasomotor rhinitis.
AUTHOR: Graf P; Enerdal J; Hallen H
CORPORATE SOURCE: Department of Otorhinolaryngology, Huddinge University Hospital, Karolinska Institute, Stockholm, Sweden.
SOURCE: Archives of otolaryngology--head & neck surgery, (1999 Oct) Vol. 125, No. 10, pp. 1128-32.
Journal code: 8603209. ISSN: 0886-4470.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 27 Oct 1999

L8 ANSWER 13 OF 16 MEDLINE on STN
TI Rhinitis medicamentosa: aspects of pathophysiology and treatment.
AB With modern vasoconstrictors, such as oxy- and xylometazoline, the risk of developing rhinitis medicamentosa (RM) has been considered to be small or even nonexistent. However, recent studies have shown that overuse of these drugs may result in rebound congestion, nasal hyperreactivity, tolerance, and histologic changes of the nasal mucosa. Using rhinostereometry, it has also been shown that the long-term use of the preservative benzalkonium chloride (BKC) in oxymetazoline nasal spray accentuates the severity of rhinitis medicamentosa in healthy volunteers. A nasal decongestant spray composed of a combination of vasoactive substances and BKC has a long-term adverse effect on the nasal mucosa. BKC alone induces mucosal swelling after 30 days use of the nasal spray in healthy subjects, unlike placebo. According to the author, rhinitis medicamentosa can be defined as a condition of nasal hyperreactivity, mucosal swelling, and tolerance that is induced, or aggravated, by the overuse of topical vasoconstrictors with or without a preservative. An adequate treatment of these patients consists of a combination of vasoconstrictor withdrawal and a topical corticosteroid to alleviate the withdrawal process. The underlying nasal disorder must then be treated. Patients with rhinitis medicamentosa who overuse topical decongestants and are able to stop using such drugs should be careful about taking these drugs again, even for a few days. They must be informed about the rapid onset of rebound congestion upon repeated use in order to avoid the return of the vicious circle of nose-drop abuse.

ACCESSION NUMBER: 1998014951 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9353558
TITLE: Rhinitis medicamentosa: aspects of pathophysiology and treatment.

AUTHOR: Graf P
CORPORATE SOURCE: Department of Otorhinolaryngology, Sodersjukhuset, Karolinska Institute, Stockholm, Sweden.
SOURCE: Allergy, (1997) Vol. 52, No. 40 Suppl, pp. 28-34. Ref: 44
Journal code: 7804028. ISSN: 0105-4538.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 9 Jan 1998
Entered Medline: 1 Dec 1997

L8 ANSWER 14 OF 16 MEDLINE on STN
TI Benzalkonium chloride in a decongestant nasal spray aggravates rhinitis medicamentosa in healthy volunteers.
AB A randomized double-blind parallel study with 20 healthy volunteers was performed to research the effect of a preservative in a decongestant nasal spray on the development of rhinitis medicamentosa. Ten subjects received oxymetazoline nasal spray with benzalkonium chloride and the others used oxymetazoline nasal spray without the preservative three times daily for 30 days. Before starting the course of treatment and after its conclusion, recordings of the mucosal surface positions were made with rhinostereometry followed by histamine challenge tests. Symptoms of nasal stuffiness were estimated on visual analogue scales (0-100) in the morning and the evening just before using the nasal spray. After 30 days, rebound swelling and nasal stuffiness were found in both groups. In the group receiving oxymetazoline nasal spray with benzalkonium chloride the mean rebound swelling was 1.1 mm and the estimated mean evening symptom score for nasal stuffiness was 43. In the group without benzalkonium chloride the corresponding variables were significantly less marked, with a mean rebound swelling of 0.5 mm ($P < 0.05$) and a mean evening symptom score of 25 ($P < 0.05$). The increase in histamine sensitivity in both groups was interpreted as a sign of nasal hyperreactivity. A new type of nasal spray bottle was used that has been shown to prevent bacterial contamination. In conclusion, the long-term use of benzalkonium chloride in oxymetazoline nasal spray accentuates the severity of rhinitis medicamentosa in healthy volunteers.
ACCESSION NUMBER: 96039729 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7553241
TITLE: Benzalkonium chloride in a decongestant nasal spray aggravates rhinitis medicamentosa in healthy volunteers.
AUTHOR: Graf P; Hallen H; Juto J E
CORPORATE SOURCE: Department of Otorhinolaryngology, Sodersjukhuset, Karolinska Institute, Stockholm, Sweden.
SOURCE: Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology, (1995 May) Vol. 25, No. 5, pp. 395-400.
Journal code: 8906443. ISSN: 0954-7894.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 27 Dec 1995
Last Updated on STN: 27 Dec 1995
Entered Medline: 9 Nov 1995

L8 ANSWER 15 OF 16 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI The effect of different preparations of nasal decongestants on ciliary beat frequency in vitro.
AB Ciliated cells from the nasal mucosa of normal persons were collected in culture medium and exposed to either oxymetazoline without preservatives, oxymetazoline with preservatives, xylometazoline with preservatives, or sham (culture medium). There was a significant decrease in ciliary beat frequency only by the two drugs with preservatives after 20 min. After substitution of the test media with culture medium ciliary action did not recover in any group.
ACCESSION NUMBER: 1994:216303 BIOSIS
DOCUMENT NUMBER: PREV199497229303
TITLE: The effect of different preparations of nasal decongestants on ciliary beat frequency in vitro.
AUTHOR(S): Deitmer, T. [Reprint author]; Scheffler, R.
CORPORATE SOURCE: Univ.-HNO-Klinik Muenster, Kardinal von Galen Ring 10, D-4400 Muenster, Germany
SOURCE: Rhinology (Utrecht), (1993) Vol. 31, No. 4, pp. 151-153. ISSN: 0300-0729.
DOCUMENT TYPE: Article
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TI THE INHIBITION OF GRANULOCYTE PHAGOCYTOSIS BY VARIOUS COMPONENTS OF NASAL DROPS.
AB The effect of two decongestive substances and two preservatives used in nasal drops on phagocytosis by human granulocytes was studied. The vasoactive substances oxymetazoline chloride and zylometazoline chloride incubated with human granulocytes during 20 min. gave a reduction of phagocytosis to almost zero when using concentrations found in commercially used nasal drops (500 mg/l respectively 1000 mg/l). However, a dilution of 1:100 was consistent with an almost normal phagocytic function. The preservatives benzalkonium chloride and thiomersal gave a dose related reduction of phagocytosis down to zero. A dilution of 1:100 of the benzalonium chloride solution used commercially (200 mg/l) and a dilution of 1:10 of the thiomersal solution used commercially (24 mg/l) were needed to get an almost normal phagocytic function. These results together with previous studies indicate that the addition of preservatives in nasal drops should be questioned, excluded or replaced with other less harmful substances.
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